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A Quality Improvement Project to Assess the Value of Pharmacogenomic Testing in Adults Diagnosed with Major Depression

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Abstract

Background: Treatment of major depression follows the guidelines from evidence-based medicine established algorithms; however, 50% of patients diagnosed with major depressive disorder do not respond to their first medication trial, and 70% may go through four treatment attempts before achieving remission.

Purpose: To demonstrate the value of pharmacogenomic testing as a treatment-guidance technology in patients with resistant depression and assess healthcare providers' motivation to adopt the technology.

Methods: A retrospective chart review of (N = 73) patients' treatment response measured by the pre-post PHQ-9 depression scale after pharmacogenomic guided medication intervention with descriptive statistics and paired t-test. The project also assessed providers' motivation to adopt and use pharmacogenomic testing by completing the providers' motivation scale (PMA) before and after viewing an educational session on the subject.

Results: A significant improvement in mood with a mean decrease of 10 points in the post PHQ-9 scores ($p = .000 < .001$) in 53% of the subjects, and 33% had scores that ranked within remission. Most patients (60%) responded to 1.3 medications post pharmacogenomic treatment. The providers were motivated to learn new technology and gain knowledge derived from current information for patient care.

Conclusions: These are significant findings corresponding to the new evidence research in pharmacogenomics supporting the use of the technology as a therapeutic resource for treatment-resistant depression patients.

Keywords: *pharmacogenomics, psychiatry, major depression, nursing, innovation adoption*

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Introduction

There is a treatment gap in adult patients diagnosed with a major depressive disorder who have failed two or more medications and remain symptomatic or are considered to have treatment-resistant depression (TRD). The practice guidelines for psychiatric evaluation and treatment from the American Psychiatric Association (APA) (2015) recognize that individuals may experience an inadequate response to medications or health and mood complications due to psychotropics' adverse events. Authors like Giakoumatos and Osser (2017) and Stahl (2017) agreed that there are no treatment guidelines for patients' genotypes who failed antidepressants due to a lack of response or adverse events.

This quality improvement project compared Patient Health Questionnaire - 9 (PHQ-9) scale score changes before and after medication's guided intervention from pharmacogenomic testing (PGx) in adult patients who failed more than two antidepressants. The goal was to identify the value of pharmacogenomic testing as a personalized treatment resource in patients with genomically idiosyncratic needs vs. the non-response to treatment as usual (TAU). A second goal included the assessment of healthcare providers' motivation to adopt this technology.

Background

Major depressive disorder (MDD) has the highest prevalence in mental health conditions, with a 7.1 % among the adult population in the United States (USA) (National Institute of Mental Health, [NIMH], 2019). The results from the Sequenced Treatment Alternatives to Relieve Depression (*STAR-D*) study in 2006 showed that 50% of these individuals did not

respond to their first medication trial, and 70% of patients may go through four treatment attempts before achieving remission (NIMH, 2006). Similar findings from Warden et al. (2007) identified that less than 50% of MDD patients would achieve remission after two antidepressant trials.

The STAR*D psychopharmacology algorithm presented four levels of antidepressant management with subsequent treatment recommendations after each level's failure (Gaynes et al. 2008) (Appendix A). The first level starts with the use of citalopram. If the patient failed to respond or could not tolerate it, will switch to level two with venlafaxine extended-release or sertraline, or augmentation with bupropion sustained-release and cognitive therapy. For non-respondent individuals, level three proposed trials of mirtazapine or nortriptyline and augmentation with lithium or T3 thyroid hormone. Finally, level four recommends combining mirtazapine and venlafaxine extended-release or monoamine oxidase inhibitors (MAOIs) like tranylcypromine (Parnate).

Correspondingly, the psychopharmacology algorithm project at the Harvard South Shore Program (Appendix B) by Giakoumatos and Osser (2017) incorporates the first-line use of sertraline, escitalopram, or bupropion for the treatment of outpatient unipolar depression. If the patient does not respond, switch to a dual-action agent like venlafaxine or mirtazapine. The algorithm includes serotonin selective reuptake inhibitors (SSRIs) alone or combined with lithium or Wellbutrin for augmentation, also transcranial magnetic stimulation (TMS), supplements like omega-3s, and atypical antipsychotics. Patients who fail two antidepressants will be considered to have treatment-resistant depression (TRD). The group guidelines suggest reviewing the patient’s history, symptoms, past responses, comorbidities, family history, and

preferences before a third medication trial (APA, 2015; Giakoumatos & Osser, 2017; Stahl, 2017).

Polypharmacy is a practice that has increased in psychiatry over the last 20 years (Shrivastava, 2019). Treatment-resistant depression (TRD) patients are frequently under psychiatric polypharmacy with two or more prescriptions unless discontinuing a medication due to adverse effects. The use of more than one medication increases drug interactions, potential adverse effects, morbidity, and mortality (Sarkar, 2017). Johnston et al. (2019) and Mrazek et al. (2014) found in a systematic literature review that TRD patients who have failed more than two medication courses will experience a reduced health-related quality of life (HRQoL). According to the authors, these patients will also have higher relapse rates, increased mortality, and additional medical direct and indirect costs to society of $29 to 48 billion dollars a year.

The science of pharmacogenomics has been evolving since the 1960s, intending to find genetically congruent medications based on the individual's genetic markers or metabolic profile (Charlab & Zhang, 2013). Different medical specialties, including psychiatry, benefit from pharmacogenomics to identify patients' metabolic biomarkers with strengths or weaknesses in the Cytochrome P-450 (CPY450) family (pharmacokinetics), and variations in genetic morphology receptors (genotype) that may affect drug response and result in SSRI resistance (Vadodaria et al., 2019).

Currently, the Food and Drugs Administration (FDA) recognized four genes evidence-based verified pertinent to psychopharmacology, cytochrome P450 2D6 (CYP2D6), cytochrome P450 2C19 (CYP2C19), human leukocyte antigen, B type, allele 15:02 (HLA-B*15:02), and human leukocyte antigen, A-type, allele 31:01 (HLA-A*31:01), (Hicks et al., 2016; Miller, 2019). There is plenty of controversy around the use of pharmacogenomic testing frequently

elicited by companies that advertise the test will predict medications for an individual. Recent and ongoing clinical trials show that pharmacogenomic testing (PGx) offers patients congruent medication alternatives compatible with their genotype needs.

Review of the Literature

This review of the literature explored pharmacogenomic testing as an alternative to guide the treatment of patients who have failed two or more antidepressants. Search engines from 2014 to 2020 included the Cumulative Index of Nursing and Allied Health Literature (CINAHL), PubMed Central of the National Library of Medicine, and Google Scholar for the medical subject headings (MeSH): *pharmacogenomics, psychiatry or psychiatric or mental health, nursing, clinical guidelines, randomized controlled trials, and systematic reviews.*

Inclusion criteria followed the levels of evidence I to II recommended by the National Guideline Clearinghouse (U.S. Department of Health and Human Services, n.d.), focusing on randomized controlled trials (RCT), clinical guidelines, controlled studies, prospective and retrospective studies, and systematic reviews. The exclusion criteria was comprised of level IV editorials, letters, opinion articles, six duplicated articles, and two ongoing pharmacogenomic clinical trials in Europe and Oregon, United States.

Most articles were available through the University of Massachusetts EBSCO host database. The search revealed 47 articles in the time frame for pharmacogenomics and psychiatry or psychiatric or mental health and randomized controlled trials. The final selection included 15 articles: the guidelines from the Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Dutch Pharmacogenetics Working Group, five Level I RCTs comparing treatment as usual vs. pharmacogenomic testing, one review of three randomized controlled trials, one open-label prospective study, one case-control study, and three systematic

reviews. There were no results under pharmacogenomics and psychiatric nursing, and randomized clinical trials. However, for the terms “nursing and clinical trials,” six nursing articles included two Level IIB quasi-experimental retrospective studies, both covered in this review.

Clinical Guidelines

The U.S. Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Dutch Pharmacogenetics Working Group in the Netherlands share therapeutic recommendations for the dosing of antidepressants, including tricyclics (TCAs) and Selective Serotonin Reuptake Inhibitors (SSRIs) (Bank et al., 2018; Fabbri, & Serretti, 2019). All clinicians who prescribe will benefit from the guidelines recommendations appropriate for patients with genotype variances (Hicks et al., 2015, 2016).

The guidelines identified two essential pharmacokinetic genes involving the metabolism of most antidepressants (TCAs and SSRIs) based on levels of evidence I and II, cytochrome P450 2D6 (CYP2D6) and cytochrome P450 2C19 (CYP2C19) (Bank et al., 2018; Hicks et al., 2015, 2016). The classifications of genotypes are normal, intermediate, ultra-rapid, and poor metabolizer. Both consortiums agree on the need for dose adjustment when prescribing antidepressants to patients identified as ultra-rapid and poor metabolizers or consider an alternative medication (Bank et al., 2018; Hicks et al., 2015, 2016). Lack of knowledge of the patient's possible genotype variants will result in the prescriber's treatment as usual (TAU) choices, perpetuating the potential failure, adverse events, or inappropriate polypharmacy.

Evidence-Based Psychopharmacology

Greden et al. (2019), in a rater patient-blind randomized controlled trial (RCT) of treatment as usual (TAU) medications vs. the pharmacogenomic guided intervention (GUIDED)

with N = 1167 MDD patients, found the guided group had significant results for response and remission rates p = 0.013 and p = 0.007 respectively. However, results were not significant for symptom improvement, possibly since some TAU group patients were already taking genetically congruent medications. In a post hoc analysis of the GUIDED data, Dunlop et al. (2019) found significant improvement, response, and remission rates at eight weeks using the Hamilton Depression scale 6 (HAM-D6) in patients in the GUIDED group and the TAU group with the prescription of personalized medications.

In a Level I RCT for outpatient and inpatient Spanish public hospitals, Pérez et al. (2017) found that MDD patients in the pharmacogenomic guided group had a higher response and better tolerability to antidepressants than TAU groups, but not sustained response. In China, Xiao-Xiao et al. (2019) had comparable results in a Level II case-control trial. Individuals identified by testing with the *ABCB1* TT genotype of rs2032583 improved treatment response to selective norepinephrine reuptake inhibitors (SNRIs).

Contrary to the previous results, Ruaño et al. (2020) randomized patients' treatment at the Institute of Living at Hartford Hospital based on their CYP2D6 genotype vs. TAU to compare the length of stay (LOS) and readmissions rate (RAR) between groups. They found no statistical differences between groups; however, the authors identified genetic polymorphisms in the study population and recognized the barrier of physicians' non-compliance with pharmacogenomic test recommendations. Solomon et al. (2019) had similar inconsistent findings for treatment response or improved clinical outcomes in PGx testing of CYP2D6 and CYP2C19.

A pragmatic randomized controlled trial by van der Schans et al. (2019) tested CYP2D6 in depressed elderly patients to determine the benefits of accelerating nortriptyline or venlafaxine dose vs. non-pharmacogenomic testing (PGx) controlled group and a normal CYP2D6 group.

The researchers found no significant mean time differences between groups to reach adequate doses. However, more patients (n = 24) in the genotyped group who were poor and intermediate metabolizers (PM, IM) reached medication levels vs. the control group (n = 16). The researchers also found lower adverse events in the external control group (normal metabolizers) than the genotype groups. The findings reflect the benefits of PGx for appropriate dosing in individuals with PM or IM genotypes in accordance with the clinical guidelines.

In a review of three Level I RTCs, Altar et al. (2015) evaluated pharmacogenomic guided medication versus treatment as usual (TAU) based on Hamilton – Depression 17 (HAM-D17) and Beck Depression Inventory (BDI), respectively. Findings showed that patients with pharmacogenomic guided treatment had a 2.3 higher odds ratio of clinical response than patients in TAU. Congruent with these, Tanner et al. (2018) found in a Level II open-label prospective study that patients with moderate to severe depression had a 31% greater improvement in response and 15.2 % greater remission rates when using pharmacogenomic testing.

There are two Level II pharmacogenomic testing studies in recent nursing literature. One is a quality improvement pre – post test design by Conley et al. (2020) using pharmacogenomic testing in the psychotropic management of patients with chronic mental illness. The researchers found that patients with psychotropics guided by PGx decreased symptoms, increased treatment engagement, and improved community function. In a retrospective six-month pre-post chart review of patients guided medications adjustments post pharmacogenomic testing, White et al. (2018) identified patients improved tolerability and decreased side effects.

In systematic reviews of pharmacogenomic testing for patients' outcomes, benefits, and testing cost-effectiveness, Peterson et al. (2017) and Rosenblat et al. (2017) found mixed evidence of cost-effectiveness and improved health outcomes in the literature. The researchers

agreed that there were few pharmacogenomic randomized controlled trials before 2018, therefore limited evidence. On the other hand, a retrospective cohort study from Sussman et al. (2019) established the cost benefits of using pharmacogenomic testing with potential health care savings of over $3,000.00 dollars a year in individuals with treatment resistant depression.

The validity and utility of pharmacogenomic testing in recent research illustrates the improved response and remission rates for depression in patients with genotype deviations. It also showed the opportunity to anticipate medication dosing, drug-gene interactions, response deficits, or side effects (Benitez et al., 2015). The Food and Drug Administration (FDA) recognizes pharmacogenomics' use to identify individuals who will or will not respond to medications, avoid adverse events, and improve drug response (FDA, 2020). Their guidelines include drug labeling with data enforcing risks in drug exposure and adverse events, genotype dosing recommendations, drug mechanisms, and drug target and disposition genes (FDA, 2019). The agency also bounds pharmacogenomic testing companies from making false claims or advertisements for predicting patient–medications response (FDA, 2019).

Theoretical Framework

The Diffusion of Innovation Theory by Everett Rogers (2003), provided the ground for this DPN project (Appendix C). The communication model promotes the adoption of new behaviors or ideas by the target groups, in this case, health professionals, organization leaders, and patients. Rogers (2003) recognizes that the acquisition of ideas in a population takes time for its adoption, and individuals will join at different times based on their needs and personal characteristics.

According to Rogers (2003) the five categories of innovation adopters are: innovators, early adopters, early majority, late majority, and laggards. All will go through the stages of awareness, the decision to adopt or reject, initial use, and continued use of the innovation at their own pace. The individual's choice to adopt the new idea will be based on five factors: 1) the belief that the new idea is better than the old; 2) the idea must be consistent with the adopters' values and needs; 3) level of difficulty to understand or use; 4) testing capability; 5) observable results – outcomes (Rogers, 2003).

The diffusion process requires knowledge to engage, persuade, and maintain change (Rogers, 2003). In a systematic review of oncology physicians' genomic literacy, Ha et al. (2018) examined Rogers' three types of knowledge in the translation and adoption process: awareness, how-to, and knowledge principles. Their findings reflected that 87% of these physicians had an awareness of the different cancer genetic assays, but only 20 to 40% were ordering the assays. This data confirms that awareness is not tantamount to applying new technology.

The slow adoption of pharmacogenomic testing by healthcare providers is an ongoing debate that resonates with the Diffusion of Innovation Theory. Some scientific groups are in support, while others prefer to continue with the traditional treatment as usual or TAU until more evidence is available. In a meta-data analysis of 36 studies, Veilleux et al. (2020) found that physicians were not ordering pharmacogenomic testing due to recognizing their knowledge deficits in the topic. This project included an education component to promote providers with an evidence-based understanding of pharmacogenomics and the conviction that PGx testing adoption leads to improved patient care.

Methods

This quality improvement program did a record review in a community mental health agency in Western Massachusetts of their current use of pharmacogenomic testing to identify patients' response and remission to genetically sound medications measured by the Patient Health Questionnaire 9 (PHQ-9). The project also surveyed providers' motivation to adopt pharmacogenomics before and after an educational presentation to motivate and strengthen their adoption and knowledge in using the technology.

The timeline (Appendix D) started in October 2020 with a two-year retrospective chart review from November 2018 to October 2020 of patients diagnosed with major depression (MDD) who received pharmacogenomic testing. Next, providers including physicians, nurses, administrators, and a group of therapists received a Survey Monkey consent via email to participate in the project (Appendix E), and if acceded, continued to the Provider Motivation Adoption (PMA) Pre-scale (Appendix F). The scale measures motivation to adopt and maintain the use of innovative technology (Hatz et al., 2017). During November 2020, the providers received a 15 minutes video powerpoint education in pharmacogenomics and related literature (Appendix G). A post-survey (Appendix H) was available to the providers and staff during February 2021.

For the chart review, the inclusion criteria were adults over 18 years old diagnosed with MDD, a history of two or more medication failures, and previous pharmacogenomic testing at the agency. Exclusion criteria were patients with other diagnoses (e.g., bipolar disorder), concurrent transcranial magnetic stimulation treatment (TMS), or drop out from treatment before guided intervention.

This project did not require a budget investment by the agency since the data is already

part of the electronic medical record (EMR), and providers could fill the PMA scales online. The education program was a 15 minutes video PowerPoint delivered by email to watch in their own time. Using the electronic platforms provided access and saved the cost of materials.

Goals, Objectives, and Expected Outcomes

The project's main goal was to assess the value of pharmacogenomic testing in the psychotropic management of adults diagnosed with major depressive disorder (MDD) who have failed two or more medications. A secondary goal was to promote the adoption and use of pharmacogenomic testing by medical providers. To achieve this, the student followed these objectives (Table A1):

1. Evaluated the response to pharmacogenomic guided medications in patients tested from 2018 to 2020 with the Patient Health Questionnaire - 9 scales by February 2021.
2. Assessed providers' motivation to adopt pharmacogenomic testing with the provider motivation adoption scale (PMA scale) (Hatz et al., 2017) during November 2020.
3. Promoted providers' adoption of pharmacogenomic testing with education on the topic by November 2020.

The expected outcomes were greater efficacy in treating depression in the project subjects as evidenced by improved treatment response with a minimum drop in five points from baseline in the Patient Health Questionnaire - 9 scale, or remission with four or less total points on the scale. The secondary outcome expected and increased in provider motivation to use pharmacogenomic technology measured by an increase in the PMA scale results after the education in the topic.

Project Site and Population

A community mental health agency in Western Massachusetts was the site for this project. The agency serves a diverse population of over 12,000 individuals and families from different socio-economical, racial, and cultural backgrounds. The agency is composed of multidisciplinary mental health professionals who offer a variety of behavioral and psychopharmacology modalities. In 2018 the medical director incorporated pharmacogenomic testing for medication guidance in patients non-responsive to treatment, and in 2019 added the Transcranial Magnetic Stimulation (TMS) program.

The medical team comprises psychiatrists, child psychiatrists, primary care physicians, advanced practice nurses, and registered nurses. Providers follow treatment as usual (TAU) medication protocols based on major depression (MDD) guidelines. Pharmacogenetic testing is available in the agency and covered by MassHealth, Medicaid, Medicare, and some commercial insurances. However, due to providers' time limitations with a high volume of patients and possible knowledge gaps in using the pharmacogenomic report, the testing is not used as a standard practice in treatment resistant patients who failed the recommended algorithms.

Description of the Group

The retrospective review's target population was 123 records of adults diagnosed with MDD who failed at least two antidepressants and had pharmacogenomic testing from November 2018 to October 2020. The providers' educational intervention included four physicians, five nurses, three administrators, and a group of 15 randomly selected psychotherapists. The group received via email a Survey Monkey consent to participate in the project (Appendix E), and if acceded, continued to the Provider Motivation Adoption (PMA) Pre-scale (Appendix F) and video education program.

Measurement Instruments

For the record review, patients had filled the self-assessment Patient Health Questionnaire - 9 (PHQ-9) (Appendix I) ideally on their first interview and during treatment. The PHQ-9 is an ordinal scale that assesses degrees of depression. Scores ranging between 5 - 9 are mild symptoms, and scores ranging from 10 – 27 are considered depression from moderate to severe. Levis et al. (2019) found a combined sensitivity of 0.88 and specificity of 0.85 for a cut-off score of 10 or above.

The educational session and assessment of motivation, providers were engaged in the project during the monthly zoom team conference and received by email a pre and post-test based on the Physician Motivation Adoption (PMA) scale from Hatz et al. (2017) (Appendix F, Appendix H). The PMA scale is a five-point Likert scale that measures physicians' motivation to adopt different medical technology or devices (Hatz et al., p. 533). It has excellent reliability and validity with an acceptable Kaiser-Meyer-Olkin (KMO) test value of 0.76. For this project, and after obtaining authorization from the author (Appendix J), the scale was renamed the Provider Motivation Adoption scale to allow non-physician providers to participate in this project (Advanced Practice Nurse, Nurses, clinicians, and administrators). The PMA scale was labeled as Pre-PMA (Appendix F) for the initial assessment and Post-PMA (Appendix H) after the educational intervention with additional comments option in both.

Providers Education Program

Due to Covid quarantine and providers' availability limitations, the DNP student submitted by email a video education program in pharmacogenomics (Appendix G) for the agency providers, including psychiatrists, nurses, and therapists, after the online pre-test assessment. The content included definitions of pharmacogenomics, clinical guidelines, FDA regulations, and

strategies to understand the pharmacogenomic report's clinical application. The presentation combined various sources, including authorized material from the Neuroscience Education Institute in California, USA (Appendix K). After one to two months from the video education, the providers received the post-PMA via SurveyMonkey email link.

Data Collection and Analysis

The data was collected from patients' pharmacogenomic reports at the Myriad AssureRx secure website, the PHQ-9 scores, and their demographic data from the electronic health records. Thirty subjects were missing PHQ-9 scales and called to update their information. The input was organized in an excel sheet and transferred to the Statistical Package for Social Sciences (SPSS) program (Appendix L). The statistics included patients' demographics (age, gender, race-ethnicity), changes in mood response or remission based on PHQ-9 scales pre-post pharmacogenomic guided treatment, number of medications before and after the PGx guided report, comorbid personality disorders (borderline personality disorder and history of substance use), and genotype report data (e.g., CPY450 variations).

The analysis included descriptive statistics of the group demographics, an average of medications before and after pharmacogenomic testing, comorbid borderline personality disorder vs. history of substance use responses, and genotype findings. Paired t-test was used to examine the difference between PHQ-9 scores before and after pharmacogenomic guided medication. Due to sample size limitations and cross-over comorbid diagnoses within the sample subjects, inferential statistics were not appropriate. Nonetheless, crosstabulation allowed to examine the relation of post-PHQ-9 scores and subjects with comorbid borderline personality disorder and substance use history.

The providers' motivation data were obtained from their responses to the PMA pre-post scales via SurveyMonkey on their website under the student's secure account. Descriptive statistics described their responses and motivation to adopt the new technology after the education intervention.

Ethical Considerations and Protection of Human Subjects

To comply with the University of Massachusetts, Amherst (UMass) Internal Review Board (IRB), the student obtained the agency approval for the Quality Improvement Project for the retrospective chart review (Appendix M). The agency providers received a consent form for their participation in the PMA survey in early November 2020. The pharmacogenomic reports from Myriad AssureRx are the product the agency uses. The student discloses no bias or conflict of interest in the pharmacogenomic report or the company.

The Health Insurance Portability and Accountability Act ([HIPPA], 2003) requirements for retrospective studies emphasize the use of patient non-identified data. Therefore, patients' data were assigned a number in the pharmacogenetic reports, PHQ-9 scales, patients' diagnoses, and demographics. The student destroyed any list of cases after the data was collected. All electronic files containing identifiable information are password protected to prevent unauthorized users' access, and only the project coordinators have access to the passwords.

The nursing Code of Ethics standards reiterate the nurse's responsibility to guarantee the patient's interests, safety and protect their rights (Winland-Brown et al., 2015). The student guaranteed the patient's and staff's best interests, protected their confidentiality and safety during this review by avoiding any identifiable information and protecting the project's data.

Results

The record review was completed between October 2020 to February 2021. It included 123 records of adults over 18 years old diagnosed with major depressive disorder (MDD) who failed more than two antidepressants and had pharmacogenomic testing (PGx) for treatment guidance. The final sample consisted of 73 cases that met the inclusion criteria. Patients with a diagnosis of bipolar disorder (16), in concurrent transcranial magnetic stimulation TMS (10), and closed before followed PGx treatment (24) were excluded. The providers' survey, including video education, was emailed to 27 physicians, nurses, clinicians, and administrators, out of which 12 responded to the Pre-PMA survey, and only three responded to the Post-PMA survey despite reminders by email.

Record Review Demographic Characteristics

The 73 patients diagnosed with major depression ages ranged from 18 to 71, with a mean age of 44 years old. A majority (72.6%) were females and 27.4% males, predominantly White European-American 86.3%, with White Hispanic 8.2%, and 5.5% Black African-American.

Before pharmacogenomic testing, 17 patients (23.3%) had an average of four medications, 16 (21.9%) had eight to eleven medications, and 15 (20.5%) had five to seven medications. The average number of medications after pharmacogenomic guided medication was 1.36 in 44 patients (60.3%), and 18 (24.7%) had two to four medications before responding to treatment.

Pre-Post PHQ-9 Scores Findings

To examine the benefits of pharmacogenomics testing, Table 2 presents the pre-post PHQ-9 depression scores after the pharmacogenomic guided medication intervention. The PHQ-9 depression scale measures depression severity where scores indicate: 0-4 minimal depression, 5-

9 mild depression, 10-14 moderate depression, 15-19 moderate to severe depression, 20-27 severe depression.

Table 2

PHQ-9 Pre – Post and Difference Scores

	Pre PHQ-9 score	Post PHQ-9 score	Difference PHQ-9 scores
N	64	65	63
Mean	18.95	9.08	10
Std.Deviation	4.18	6.25	5.60
Median	19.50	7	12
Mode	22	5	13

The post-PHQ-9 produced a mean of 9.08 points with 6.25 standard deviations (SD) vs. a pre-PHQ-9 mean of 18.95 with 4.18 SD. This represents a mean difference or decrease of 10 points in the post-measurement or treatment response with more than five points decrease. Interestingly, the post scale (n = 65) has a mode or most frequent score of five points (minimal depression) in 13.7% of the group vs. a previous mode of 22 (severe depression) in 12.3% of the subjects in the pre-PHQ-9. It must be noted there were nine missing values in the pre-data and eight missing in the post-scores. The discrepancy resulted from the PHQ-9 scale not being part of the agency's routine measurements for all patients; therefore, not all subjects had the scale before or after the PGx testing. For this reason, the analysis follows the reported data from SPSS. Nonetheless, the missing values, the sample of 64 subjects in the pre-PHQ-9, has a normal

distribution with a Pearson's coefficient of skewness Sk2 = -.39 (-0.5 to 0.5 approximately symmetric).

To further assess the difference between the pre-post PHQ-9 scales, a paired t-test was used with results presented in Table 3.

Table 3

Paired Samples Test

Pair 1	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper	t	Df	Sig. (2-tailed)
Pre-PHQ-9 Score Post-PHQ-9 Score	10	5.605	.706	8.588	11.412	14.412	62	.000

Note. Correlation r =.488

The paired t-test for the pre-post PHQ-9 scores revealed a moderate association with a correlation of r=.488, indicating a positive change between the scales where scores decreased linearly after the pharmacogenomic intervention. The data reflects a statistical mean difference with significant p=.000 < .001, which reveals patients' response to treatment with a significant decrease of 10 points mean in the post PHQ-9 scores or treatment response (5 – 9 mild depression) after the pharmacogenomic guided medication changes. The results do not suggest remission due to most of the scores in the "5-9 mild depression and 10-14 moderate depression " values in the post scale.

This project did not include patients with multiple comorbid diagnoses (e.g., anxiety, post-traumatic stress), except subgroups with a diagnosis of borderline personality disorder (BPD) and substance use, as illustrated below in Table 4.

Table 4

Gender Comorbid Borderline Personality and History of Substance use

	Gender			
	Male		Female	
	N	%	N	%
No Comorbid Diagnosis or Substance Use	3	4%	22	30%
Substance Use Hx[a]	14	19%	25	34%
Borderline Personality Disorder[a]	4	5%	15	20%
Borderline Personality & Substance Use Hx[a]	4	5%	8	10%

Note. N = 73

[a]Some of the percentages exceed 100% due to overlap.

A subgroup with the diagnosis of comorbid borderline personality disorder (BPD) was identified in 26% of individuals. Twenty percent were females with predominant ages of 29 to 39 and 51 to 50 (n=6 in each age subgroup). In terms of comorbid borderline personality disorder and substance use history, the results identified eight (10%) of females with comorbid personality diagnosis and substance use history. There were four (5%) males diagnosed with BPD and four (5%) with combined BPD and substance use history. The more significant number of females in the sample and the fact that they have diagnosed BPD 3:1 ratio to males are portrayed in the results.

There was a past substance use history in 39 (53%) of the 73 patients, which included alcohol and cannabis and/or cocaine and/or opiates (19.2%,) cannabis (8.2%,), opiates (6.8%), cocaine (1.4%), opiates and cannabis (1.3%), and active cannabis use (11.8%). In the gender subgroups, 19% of the males, half of the subgroup, had past substance use vs. 34% of the females. The "National Survey on Drug Use and Health" by McCance-Katz (2019) identified 19.3 million Americans over 18 years old with a substance use disorder (SUD), 20.6 million with a mental illness, and an overlap of 9.5 million individuals with both SUD and mental illness. The sample data had a higher proportion; more than half of the patients had a SUD history, probably due to the sample size limitation.

To explore any relation in the post PHQ-9 scales of patients with comorbid BPD or substance use history vs. no comorbidities, Table 5 shows a crosstabulation.

Table 5

Post PHQ-9 in Patients With no Comorbidities vs. BPD and Hx. SUD

Post PHQ-9 scores	No Comorbid Diagnosis[a]		Borderline Personality Disorder[a]		History of Substance Use[a]	
	N	%	N	%	N	%
0 – 4	14	21%	1	1.5%	7	10%
5 - 9	15	23%	9	13%	12	18%
10 – 14	10	15%	2	3%	6	9%
15 - 19	4	6%	3	4%	2	3%
20 - 27	2	3%	4	6%	6	9%

Note. N=65. Missing values.
[a] Subjects and percentages may overlap

All three subgroups had most subjects post PHQ-9 scores in the “5 – 9 mild depression” range with a highest 23% in the “no comorbid diagnosis,” 18% “history of substance use,” and the lowest 12% in “borderline personality disorder.” We can observe 21% and 10% of “0 – 4 none to minimal depression” or remission in the “no comorbid diagnosis” and “history of substance use” subgroups. The patients in the history of substance use had more scores 10% > 1.5% in the “0 – 4 none to minimal depression” and 18% > 12% in the “5 – 9 mild depression” than the BPD subgroup. The findings indicate that individuals in the borderline personality disorder subgroup had lower responses post pharmacogenomic intervention.

Other interesting findings included the subjects' genotypes for the serotonin transport gene SLC6A4 with a 45.2% L/S variant "Intermediate Sensitivity" and a 27.4% S/S variant with "Increased Sensitivity." These variants will result in decreased serotonin transport and reduced response to SSRIs antidepressants. The serotonin receptor genes HTR2A A/A had a 15.1% and the HTR2A G/G a 39.7% of the subjects. In both cases, evidence research demonstrated 15% and 42% of potential side effects to SSRIs, respectively. Table 6 below presents the sample findings for the cytochrome P450 enzyme system's responsible for metabolizing most substances and medications.

Table 6

Sample Distribution Cytochrome P450 Enzymes

	CYP 1A2	CYP 2B6	CYP 2C19	CYP 2C9	CYP 2D6	CYP 3A4	UGT 1A4	UGT 2B15
Normal	46.6%	56.2%	68.5%	63.0%	61.6%	83.6%	75.3%	78.1%
Intermediate Metabolizer	2.7%	37.0%	20.5%	35.6%	19.2%	16.4%	2.7%	21.9%
Poor Metabolizer	0.0%	5.5%	2.7%	1.4%	11.0%	0.0%	0.0%	0.0%
Ultrarapid Metabolizer	50.7%	1.4%	8.2%	0.0%	8.2%	0.0%	21.9%	0.0%

Note. N = 73

The most common genotypes in the sample (50.7%) were with the ultrarapid (fast metabolizer) enzyme CYP1A2. This finding is not relevant for our discussion since the enzyme is not responsible for metabolizing antidepressants. However, it is the main pathway for medications like Clozaril, Zyprexa, and others (Flockhart, 2008) to treat psychosis and schizoaffective disorders.

The following frequent group was in the "intermediate metabolizer" (IM) category with 37% for the CYP2B6 enzyme responsible for the antidepressant bupropion (Wellbutrin), and the CYP2C9 enzyme 35.6%, which participates in the metabolism of amitriptyline (Elavil), doxepin (Sinequan), fluoxetine (Prozac), venlafaxine (Effexor), and valproic acid (Depakote) (Flockhart, 2008). The enzyme CYP2C19, which metabolizes citalopram and escitalopram (Celexa and Lexapro) and several TCAs, had a 20.5% IM, and UGT2B15, which metabolizes sedatives often used in depressive disorders, had 21.9% IM.

Finally, 19.2% of the patients were "Intermediate Metabolizer" and another 11% "Poor Metabolizer for the enzyme CYP2D6, which metabolizes 25% of all prescription drugs and many antidepressants like Prozac, Paxil, Cymbalta, Effexor, and TCAs. The awareness of these genotype deficiencies in a population will help prescribers dose antidepressants according to clinical guidelines to prevent adverse reactions in individuals who are intermediate or poor metabolizers or avoid drugs metabolized by those enzymes.

Participants Motivation to Adopt

Another piece of this evaluation was getting the participants (physicians, nurses, administrators, and clinicians) to complete the Provider Motivation Adoption Scale (PMA scale) regarding their motivation to use new technology in their work. The motivation to the adopt scale was sent to a group of clinicians and administrators during November 2020. Of the 27 healthcare professionals, only 12 responded to the Pre-PMA survey, with only eight surveys complete enough to use the data.

Of the 12 that responded: 12.5% were physicians, 25% nurses, 25% administrators, and 37.5% clinical therapists. Their ages range from 55 to 64 with 62.5%, 35 to 44 with 25%, and 45 to 54 with 12.5%. Sixty-two percent (5) of the respondents were females, 25% male, and 12.5% "other" gender. Although only one prescriber was in this group, many were nurses who could influence care decisions. Two were administrators who could influence policy and **f**inancial expenditures in the organization. Despite having a small number of respondents, some interesting data emerged as presented in Table 7.

Table 7

Providers Pre-Motivation Adoption Scale

Items		Strongly Disagree (1)	Disagree (2)	Neutral (3)	Agree (4)	Strongly Agree (5)
Functional						
F1	Reliability	0.0%		50.0%	25.0%	
F2	Time Saving	0.0%		62.5%	25.0%	
F3	Practical	0.0%		62.5%	12.0%	
F4	Facilitation	0.0%		62.5%	0.0%	
Conformity						
Con1	Expectations	12.5%	50.0%	0.0%	0.0%	
Con2	Advice	12.5%	50.0%	0.0%	0.0%	
Con3	Utilization	0.0%	50.0%	12.5%	0.0%	
Con4	Competition	25.0%	25.0%	12.5%	0.0%	
Con5	Majority opinion	12.5%	12.5%	50.0%	0.0%	
Power						
P1	Recognition	12.5%	25.0%	12.5%	0.0%	
P2	Career advance	25.0%	50.0%	0.0%	0.0%	
P3	Opinion leader	12.5%	37.5%	12.5%	0.0%	
P4	Decision makers	12.5%	50.0%	25.0%	12.5%	
P5	Future earnings	12.5%	50.0%	0.0%	0.0%	
P6	Pioneer	0.0%	37.5%	50.0%	12.5%	
Hedonic						
H1	Passion	0.0%	50.0%	25.0%	0.0%	
H2	Satisfaction	0.0%	25.0%	75.0%	0.0%	
H3	Excitement	0.0%	0.0%	75.0%	25.0%	
H4	Joy	0.0%	12.5%	87.5%	0.0%	
H5	Enthusiasm/personal reward	0%	50.0%	50.0%	0.0%	
Patient Benefit						
PB1	Despite High Cost	0.0%	25.0%	37.5%	37.5%	
PB2	Increased effort	0.0%	0.0%	37.5%	62.5%	
PB3	Patient well-being	0.0%	25.0%	50.0%	0.0%	
PB4	Negative recommendation	0.0%	75.0%	12.5%	0.0%	
Cognitive						
Cog1	Analytical mind	0.0%	12.5%	87.5%	0.0%	
Cog2	Intellectual challenge	0.0%	12.5%	87.5%	0.0%	
Cog3	Improve skills	0.0%	25.0%	75.0%	0.0%	
Cog4	Logical thinking	0.0%	12.5%	87.5%	0.0%	

The providers' pre-motivation scale (Table 7) revealed a 62.5 to 50% agreement to support pharmacogenomics' adoption concerning practicality, time-saving and technological reliability. The group was 50% neutral to conform expectations and utilization of PGx; at the same time, there were 37.5 to 25% in disagreement to attune to expectations and been pressured by the majority to use the technology. Similarly, they disagreed a 50 to 37.5% about the power to achieve recognition, become a key leader, and increase their earnings with pharmacogenomics' adoption. The participants were 50.0% neutral in advancing careers, impacting decision-making, and the benefit of being a pioneer in PGx.

The area of hedonics or to enjoy the adoption of pharmacogenomics technology had excellent scores with 87.5% in agreement. Seventy-five percent of the group agreed with the satisfaction and excitement of acquiring medical innovations, and 50.0% were enthusiastic about testing a medical innovation.

About patient benefits from pharmacogenomics, 62.5% strongly agreed to adopt the technology if it increases the patients' comfort. However, 75.0% were neutral about adopting the technology if there were harmful recommendations. The cognitive construct or understanding and knowledge to adopt pharmacogenomics had the highest scores with 87.5% in analysis, intellectual challenge, and logical thinking; they scored a 75.0% in the combined medical and intellectual skills. The responses in this area support the fact that clinical providers are highly motivated to pursue knowledge to improve patient care. A higher group response will be more significant to identify their preferences better.

Participants Comments

Comments received in the open text space included:

"Cost is always a concern in medical innovation."

"The interpretation of the testing is often cursory and confusing. Physicians have been trained to read diagnostic testing not as interpreters but as utilizers of bottom line data. Many insurances will not cover genomics unless failed STAR D trials from multiple categories is demonstrated."
"The conformity and power questions seem applicable for prescribers not for clinicians. A more broad and direct question like, "I support genetic testing for the best client care" would be better, in my opinion." – a clinician

Post-Participants Motivation to Adopt

Video education in pharmacogenomics was provided via email to the 27 healthcare participants. Of this group, only three people responded to the Post-PMA scale after multiple reminders. The DNP student received verbal feedback that the presentation was good but too complex, so perhaps that is why not many surveys were returned. The video education was technical in terms of the clinical use of pharmacogenomics and understanding the reports. Perhaps a series of in-person sessions after the project is complete can be developed for an extended discussion of the technology and case by case application.

Discussion

This quality improvement project's main goal was to identify the value of pharmacogenomic testing (PGx) in adult patients diagnosed with major depression (MDD) who have failed two or more antidepressants and had PGx for treatment guidance. Records review of pre-post PHQ-9 depression scale scores in 73 subjects demonstrated response to treatment with a decrease of 10 points in the scores mean. The secondary goal assessing providers' motivation to adopt pharmacogenomic testing before and after an educational intervention in the topic revealed their interest in knowledge acquisition but not motivation to adopt the technology.

The results from a convenience sample of 73 records of patients showed a predominant group of 72.6% females vs. 27.4% males, White European-American (86.3%) with an average age of 44.85 years old. There was a small representation of Hispanics (8.2%) and African-American (5.5%) subjects. These groups are a segment of the Hampshire, MA area where the U.S. census identified an 84% White (European-American), 4.01% White Hispanic, and 2.69% Black or African American (DATA USA, 2018). Brody et al. (2018) found in the U.S. National Health and Nutrition Examination Survey twice the rate of depression in women 10.4% than males with a 5.5%. The previous data and the number of females in the sample reflect that more females are diagnosed with major depression and seek treatment.

The STAR-D study data (NIMH, 2006) demonstrated that 45.2% of the subjects failed an average of four or more medications before treatment response. In synchrony with the STAR-D study, this record review found a 23% of subjects failed four medications, 21.9% failed eight to eleven and, 20.5% failed five to seven medications before pharmacogenomic testing (PGx). We can estimate that the total sum of these subgroups, 65.4% of the subjects, failed an average of six antidepressants before PGx. After the guided pharmacogenomic intervention, 44 (60.3%) of the subjects responded to an average of 1.36 medications. It is worth mentioning a subgroup of 18 (24.7%) subjects had two to four medication trials post PGx.

There was a difference of 10 points from the PHQ-9 scales pre-post mean values (Table 2 & 3) with $p = .000 < .001$ indicating subjects had a positive and significant response to pharmacogenomic guided medication. Twenty-two 22 (33%) subjects had scores within remission “0 – 4 none to minimal depression”, and 35 (53%) had “5 – 9 mild depression”. These findings are consistent with the studies from Greden et al. (2019), where 28.5% of subjects

responded to treatment, and 21.5% had remission. Similarly, Perez et al. (2017) found a higher response in PGx guided group than treatment as usual, 51.3% vs. 36.1%; alike, Tanner et al. (2018) found 31% response and 15.2% remission rates in subjects with pharmacogenomic testing.

The inclusion of the comorbid diagnoses, borderline personality disorder and history of substance use had the additional purpose of identifying these subgroups' in the treatment-resistant depression population and exploring their response to pharmacogenomic testing. Chapman et al. (2020) identified the epidemiology of the diagnosis of borderline personality disorder (BPD) with a prevalence of 1.6% in the general population, a lifetime prevalence of 5.9%, and a 3:1 ratio of females vs. males in the mental health scenarios. The subjects sample had a similar proportion of 15 females to four males diagnosed with BPD, almost 3:1 ratio.

Even though the overlap of 12 subjects in the substance use history and the BPD subgroups, the results were significantly higher 10% > 1.5% in the history of substance use subjects for remission "0 – 4 none to minimal depression", and 18% > 12% for response "5 – 9 mild depression" than the BPD subgroup. These findings serve to make a distinction between genotypic and phenotypic correlates of the phenomenology of depression. Some symptoms evolved from learned behaviors, and some symptoms stem from presumed catecholamine neurobiology. Indeed, the results support the challenges of treating comorbid borderline personality disorder (Chapman et al., 2020), requiring a multidisciplinary approach. It also suggests the use of pharmacogenomic testing may improve response to psychotropic treatment in the BPD subgroup.

The 73 subjects' phenotype findings returned a predominant White European-American (White non-Hispanic) sample representative of the local census. Dominant percentages were in

the intermediate metabolizer (IM) enzymes with CYP2B6 37%, CYP2C9 35.6%, CYP2C19 20.5%, UGT2B15 21.9%, and CYP2D6 19.2% (note CYP2D6 had the highest value 11% as poor metabolizer). A worldwide meta-analysis from Zhou et al. (2017) found a 4.3% reduced CYP2B6 in Europeans vs. 4.4% admixed Americans, reduced CYP2C9 18% European vs. 10.8% admixed Americans, reduced CYP2C19 18.5% Europeans vs. 10.7% admixed Americans, and reduced CYP2D6 29.5% European vs. 25.3% admixed Americans.

The revision results correlate with the literature review that those individuals in the poor metabolizers, intermediate or ultra-rapid groups, who already failed two antidepressants, will require medication dose adjustment or an alternative antidepressant due to their metabolic deficits (Bank et al., 2018; Dunlop et al., 2019; Greden et al., 2019; Hicks et al., 2015; Pérez et al., 2017). Furthermore, the treatment implications for the identified genotypes based on Fabbri and Serretti (2019) and their summary of the Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Dutch Pharmacogenetics Working Group in the Netherlands for the dosing of antidepressants recommend a dose decrease of 25% to 50% in individuals who are intermediate or poor metabolizers or avoid drugs processed by those enzymes.

Despite the participants' limited responses, their main areas of agreement with 87.5% to 75% were the joy to learn and test new technology and the intellectual gain and medical knowledge derived from the new information. The second most substantial areas with a 62.5% to 50% agreement were the practical time saving and reliability of pharmacogenomics and patient comfort. The group's most significant disagreement scores were 50% to 37.5% in conformity to expectations to use pharmacogenomics based on peer or social pressure, the power of receiving recognition to influence decisions, become leaders, and increase earnings from the use of the PGx.

Facilitators and Barriers

The agency administrative director and medical director were the main facilitators to support this project with the records review and staff surveys. A limitation for the record review was excluding other patients' diagnoses (e.g., bipolar disorder, anxiety disorder). A systematic review and meta-analysis from Milosavljević et al. (2021) supported genotyping for CYP2D6 and CYP2C19 for dose recommendations after associating elevated drug levels in several antipsychotics and antidepressants to individuals genotype deficits. The treatment of depression and other mood disorders often requires the concomitant use of antidepressants, antipsychotics, and other adjunct psychotropics; therefore, PGx will identify genotype deficits in the CYP 450 enzymes and other relevant genes to prevent adverse events or lack of treatment response.

There were 30 missing values from the pre-post PHQ-9 scales, a barrier to complete the data. This required contacting patients by phone to update their information and calculate their pre PHQ-9 scores before PGx from their documented symptoms in the electronic health record and patients' confirmation. The agency facilitated a team of nurses to assist with the calls to complete a meaningful sample of the scales. The timing of these calls during the current COVID quarantine and its impact on our society's social and financial changes may have contributed to higher depression scores in the post-PHQ-9 scales.

The possibility of recent PHQ-9 scores not representing the response to treatment but to the traumatic pandemic experience is both a barrier and an opportunity to use a measurement instrument. The consistent use of validated clinical instruments or measurement-based care (MBC) is believed to be less than 20% in mental health care, despite proven to substantiate assessment, monitor treatment, improve clinical outcomes, support policy decisions and

therapies reimbursement (Aboraya et al., 2018; Lewis et al., 2019). Incorporating efficient, valid, and reliable instruments for MBC is an agency clinical-policy decision that will result in the previously mentioned benefits.

There was a limitation to obtain inferential data between the subgroups of borderline personality disorder and substance use history due to their overlap. A more significant sample may exclude the overlap values to comply with inferential analysis's assumption of independence.

Several barriers may contribute to the providers' surveys' low response; the current COVID quarantine keeps most staff working from home, with increased demand for virtual work. The new virtual work reality may be an additional task and an obstacle for providers to respond to a survey and watch the video education. Other factors include the providers' perception of the complexity of understanding the pharmacogenomic technology vs. its debated reliability. Chronic time restrictions in the health system with a constraint of 15 minutes for medication follow up visits is a significant barrier to promote the appropriate use of PGx. Finally, since medical providers are the primary users of the technology, the non-medical providers may feel the technology and survey were not relevant to their needs or interest.

The previously discussed barriers to the project align with the theoretical framework of the Diffusion of Innovation Theory by Everett Rogers (2003). Individuals need time to adopt new ideas which will be influenced by their views and knowledge of the innovation attributes. Rogers states that the rate of adoption is not dependent on the awareness-knowledge of the innovation. The participants' perception of its advantage, compatibility with their work, complexity, and trialability to manage are vital factors to influence its adoption. The providers' motivation to

adopt pre-scale evidenced the participants' motivation and joy to adopt new knowledge, agreed with new technology's practicality, and patients' benefit. The low response to the post-PMA did not allow the student to identify motivation adoption changes post the video education.

Pharmacogenomic testing has been available for patients in Medicare, Medicaid, and some commercial insurances for more than ten years. Last June 2020, Medicare updated their medical necessity "Local Coverage Determination" (LCD) of pharmacogenomics testing for medications with known gene-drug interaction established by FDA or the CPIC guidelines (American Society of Health-System Pharmacists [ASHP], 2020). From a participant's comment, it is a limitation to use PGx when most insurances, particularly commercial, require the failure of more than two medications as recommended in the STAR-D multiple categories.

Healthcare cost analysis offers a realistic view of the high cost of psychiatric care related to psychotropic medication failures, including patients continuing to be depressed, unable to function in society, and the additional cost of healthcare utilization due to side effects, adverse events, or hospitalizations. The cost benefits of using pharmacogenomic testing include a potential health care savings for one individual of over $3,000.00 dollars a year with the use of genetically congruent medications (Sussman Et Al., 2019).

Finally, Rogers (2003) points that organizational decisions have a slower rate than an individual's choice. The inclusion of administrative staff in this project seeks to expand the information cascade to promote pharmacogenomic’s adoption. The final attribute of an innovation is its observability. The patients, providers, and administrators must observe the benefits of a health intervention, confirming the necessary evidence for its adoption. Therefore, the positive results from this record review of subjects' PHQ-9 scales response to treatment after

the PGx guided intervention is instrumental in demonstrating the value of pharmacogenomic testing in patients' care.

Conclusion

This DNP project evaluated the use of pharmacogenomic testing as a treatment resource for adult patients diagnosed with major depression that failed two or more antidepressants, measured by changes in the PHQ-9 depression scale pre and post pharmacogenomic guided medication. The results demonstrated a significant decrease of 10 points mean in the post PHQ-9 scores with $p = .000 < .001$ for treatment response (5 – 9 mild depression) in 53% of the subjects, and 33% had scores within remission (0 – 4 none to minimal depression). A 60.3% of patients responded to an average of 1.3 medications, and 24.7% had 2 to 4 medications post pharmacogenomic treatment. These are significant findings under the new evidence research in pharmacogenomics. The results are from the community population, which is burdened by social disadvantages, substance use, and chronic mental illness.

This project provides many opportunities to continue exploring the associated factors contributing to subjects' response to PGx: their gender, age, education, comorbid diagnosis, medications, and genotypes. Bigger sample size will provide a better representation for statistical inferences. A post-hoc analysis of some of the above variables may uncover information that was not part of the primary goal.

Time is a natural barrier in any innovation; the last ten years in pharmacogenomics research offered new evidence-based data that contribute to its diffusion of information. Providers pre-survey demonstrated their motivation and joy for new knowledge and technology toward patients’ care. The limited response to the post-survey did not allow to measure an

increased motivation to adopt pharmacogenomics. A continuous dialogue in pharmacogenomics and case discussions will be more appropriate to apply the information for clinical needs, and a more straightforward presentation for staff might be better received. The CPIC and Dutch Consortium guidelines for antidepressants and SSRIs are an excellent guide for prescribers to review medications metabolized by the hepatic P450 isoenzymes and their clinical practice implications. The guidelines apply to medication management in all medical specialties.

Nurses need to participate in pharmacogenomics clinical projects, continuing education in the technology, and assuming an active role in promoting evidence-based diagnostics and therapies that will improve patient care and safety. The agency adopted this project to continue using, evaluating, and documenting pharmacogenomic testing benefits in patients' care. The student plans to continue reporting referred patients’ responses to PGx, sharing the information within the agency clinical team and with their primary care providers, and future publication.

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Table A1

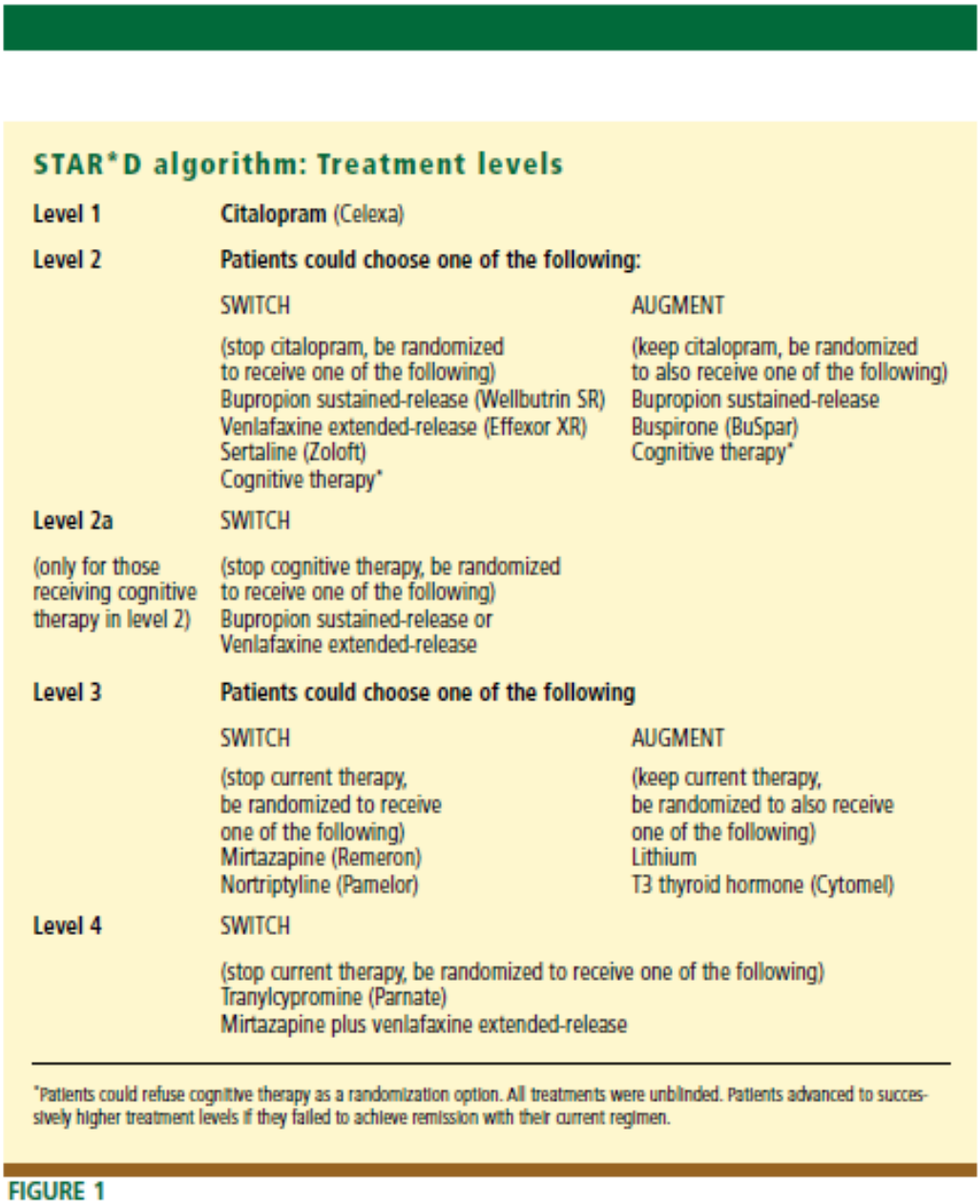
Goals, Objectives and Expected Outcomes

Goal 1: Value of pharmacogenomic testing in adults diagnosed MDD who have failed two or more medications	
Objectives	Outcomes
Evaluate response to pharmacogenomic guided medications in patients examined from 2018 to 2020 with the Patient Health Questionnaire - 9 scales.	Patients will show decreased symptoms, improved treatment response, and remission evidenced by the Patient Health Questionnaire - 9 scale with five or less points by February 2021.

Goal 2: Promote pharmacogenomic testing adoption and use in medical providers	
Objectives	Outcomes
Assess providers' motivation to adopt pharmacogenomic testing with the administration of the provider motivation adoption scale (PMA scale) by October 2020.	Establish providers' motivation baseline toward the use of pharmacogenomic testing with PMA scale by November 2020.
Promote providers' adoption of pharmacogenomic testing with education in the topic by November 2020; and re-evaluate motivation with PMA scale by February 2021.	Increase providers' motivation to adopt and use pharmacogenomic testing with education in the area, measured by positive changes in scores in the PMA scale by February 2021.

Appendix A

Star*D Algorithm



STAR*D algorithm: Treatment levels

Level 1	**Citalopram** (Celexa)	
Level 2	**Patients could choose one of the following:**	
	SWITCH	AUGMENT
	(stop citalopram, be randomized to receive one of the following) Bupropion sustained-release (Wellbutrin SR) Venlafaxine extended-release (Effexor XR) Sertaline (Zoloft) Cognitive therapy*	(keep citalopram, be randomized to also receive one of the following) Bupropion sustained-release Buspirone (BuSpar) Cognitive therapy*
Level 2a	SWITCH	
(only for those receiving cognitive therapy in level 2)	(stop cognitive therapy, be randomized to receive one of the following) Bupropion sustained-release or Venlafaxine extended-release	
Level 3	**Patients could choose one of the following**	
	SWITCH	AUGMENT
	(stop current therapy, be randomized to receive one of the following) Mirtazapine (Remeron) Nortriptyline (Pamelor)	(keep current therapy, be randomized to also receive one of the following) Lithium T3 thyroid hormone (Cytomel)
Level 4	SWITCH	
	(stop current therapy, be randomized to receive one of the following) Tranylcypromine (Parnate) Mirtazapine plus venlafaxine extended-release	

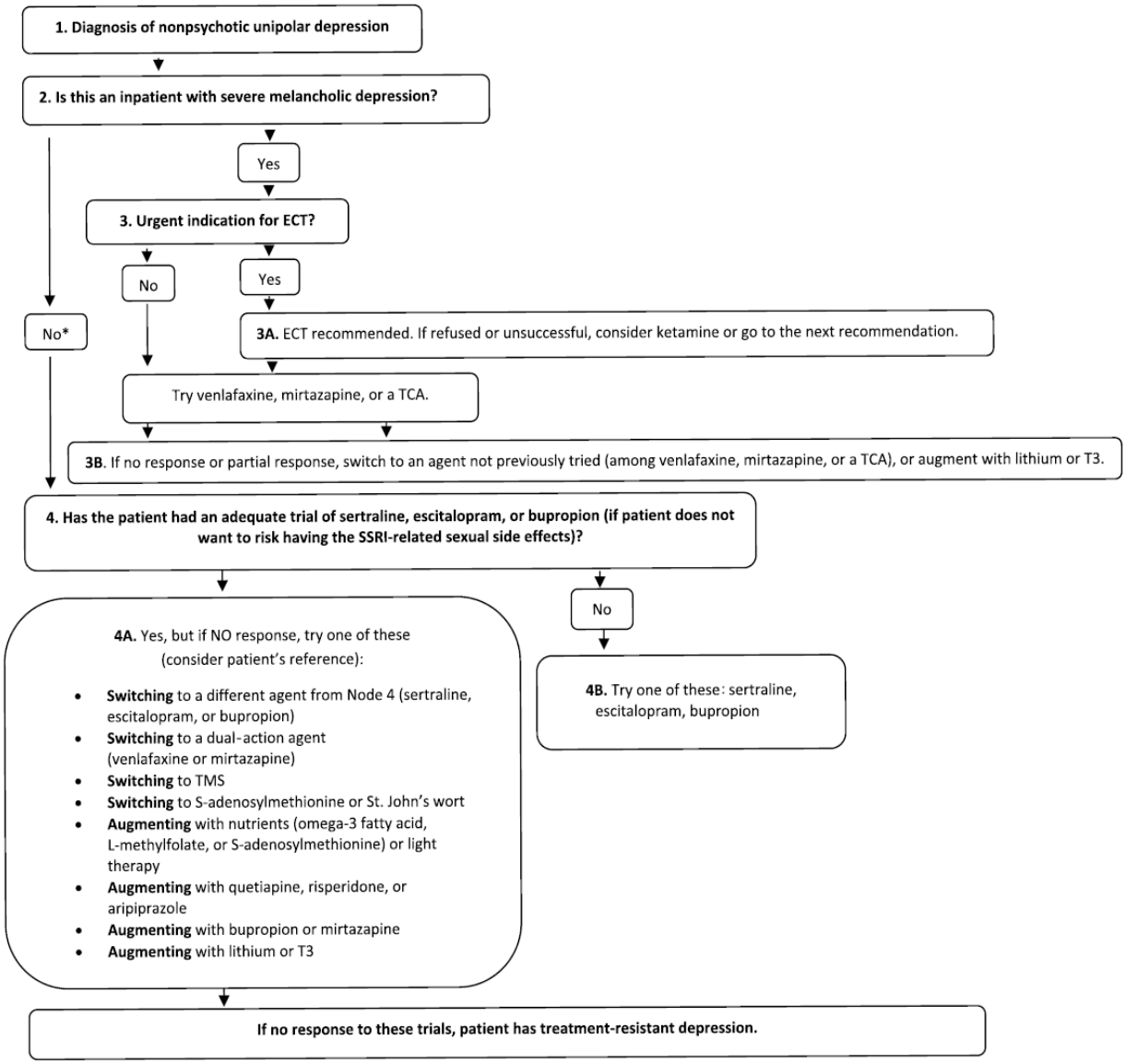
*Patients could refuse cognitive therapy as a randomization option. All treatments were unblinded. Patients advanced to successively higher treatment levels if they failed to achieve remission with their current regimen.

FIGURE 1

Source: Gaynes, B. N., Rush, A. J., Trivedi, M. H., Wisniewski, S. R., Spencer, D., & Fava, M. (2008). The STAR*D study: Treating depression in the real world. *Cleveland Clinic Journal of Medicine*, 75 (1), 57 – 66. https:// doi: 10.3949/ccjm.75.1.57

Appendix B

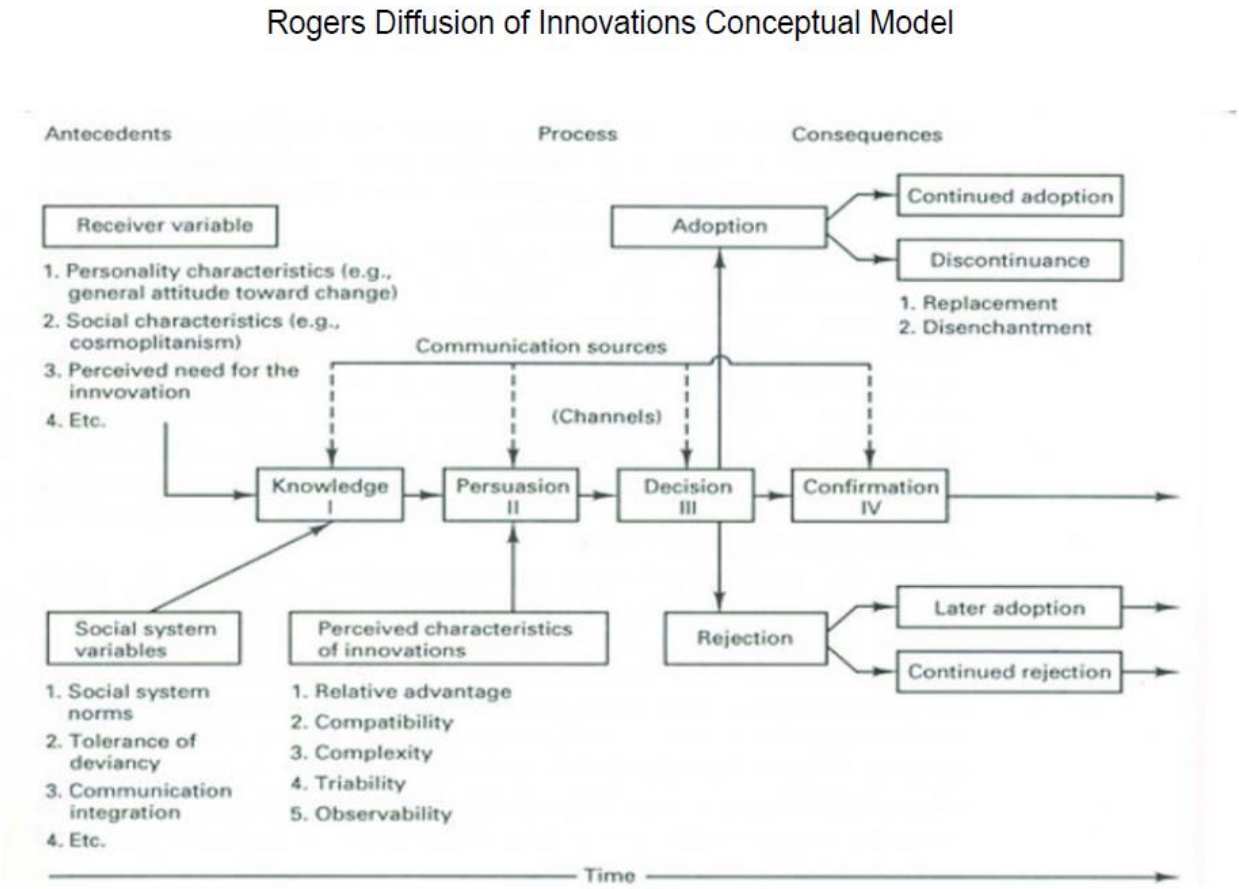
Harvard South Shore Program: Unipolar Depression Algorithm



Source: Giakoumatos, C. I. & Osser, D. (2017). The psyhcopharmacology algorithm project at the Harvard South Shore Program: An update on unipolar nonpsychotic depression. *Harvard Review of Psychiatry*, 27 (1), 33 – 52. https://doi:10.1097/HRP.0000000000000197

Appendix C

Rogers Diffusion of Innovation Conceptual Model



Source: Conceptual model of Diffusion of Innovations- Rogers, E.M. (2003). Diffusion of Innovations (5th edition). The Free Press

Appendix D

DNP Project Timeline

Fall 2020 – Spring 2021

Task	September	October	November	December	January	February	March	April
DNP project submission to UMASS IRB	X							
Submission to agency of "Waiver of Consent & HIPPA consent		X						
Started chart review of pts with PGx		X						
Send agency Providers participation consent & Pre-PMA survey		X						
Emailed Providers pharmacogenomics in-service			X					
Collected data from agency providers Pre PMA scale				X				
Analyzed initial patients' data					X			
Analyzed 1st data from agency providers						X		
Send agency providers 2nd PMA scale						X		
Collected agency providers 2nd PMA scale							X	
Analyze ALL final data							X	
Submit All data reports								X

Appendix E

Provider Agency Survey Consent Form

Provider Motivation Adoption Pre - Scale (PMA)

Provider Agency Survey Consent Form

You are being invited to participate in a Doctor in Nursing Practice translation project titled "A Quality Improvement Project to Assess the Value of Pharmacogenomic Testing in Adults Diagnosed Major Depression" done by Ileana Miranda Velazquez from the University of Massachusetts Amherst. You were selected to participate in this project because you are a health or administrative provider at ServiceNet.

The purpose of this project is to explore the value of pharmacogenomic testing in the psychotropic management of adults diagnosed major depression who have failed two or more medications.
If you agree to take part in this project, you will be asked to complete a pre & post questionnaire, first in the next page. This survey/questionnaire will ask about providers 'motivation to adopt medical innovations and it will take you approximately 5 minutes to complete. The post questionnaire will be after an education program in the next weeks. You may not directly benefit from this project; however, we hope that your participation in the education program may increase providers' knowledge and motivation to use pharmacogenomic testing.

To the best of our ability your answers in this survey will remain confidential. We will minimize any risks to breach of confidentiality by requesting only profession and demographic data, no names are requested, data will be used for project purposes only.
Your participation in this project is completely voluntary and you can withdraw at any time. You are free to skip any question you choose.
If you have questions about this project, you may contact the student, *Ileana Miranda Velazquez at imirandavela@umass.edu.* If you have any questions concerning your rights as a project subject, you may contact the *University of Massachusetts Amherst Human Research Protection Office (HRPO) at (413) 545-3428 or humansubjects@ora.umass.edu.*

By proceeding to the survey/questionnaire on the next page you are indicating that you are at least 18 years old, have read and understood this consent form and agree to participate in this project. You can print/ save this page for your records. Please DO NOT write your name on the survey/questionnaire.

1. I agree to take the survey and participate in the project.

- ◯ **Yes**
- ◯ **No**

Appendix F

Provider Motivation Adoption Pre – Scale (PMA)

Provider Motivation Adoption Pre - Scale (PMA)

Please rank the OPEN statements below based on your preference to adopt medical innovation.

1. What is your profession?

- Physician
- Nurse
- Clinical Therapist
- Administrator

2. What is your age?

- 25 to 34
- 35 to 44
- 45 to 54
- 55 to 64
- 65 to 74+

3. What is your gender?

- Female
- Male
- Other

4. Functional

I supported the adoption of medical innovation in pharmacogenomics because…

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
F1 ...is more reliable than existing technologies.	☐	☐	☐	☐	☐
F2 ...it saves time.	☐	☐	☐	☐	☐
F3 ...is more practical.	☐	☐	☐	☐	☐
F4 ...it facilitates procedures.	☐	☐	☐	☐	☐

5. Conformity

I supported the adoption of medical innovation in pharmacogenomics because...

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
Con1 ...my colleagues in my organization expect me to do so.	☐	☐	☐	☐	☐
Con2 ...my peers advise me to do so.	☐	☐	☐	☐	☐
Con3 ...all of my peers are using it.	☐	☐	☐	☐	☐
Con4 ...the competitive environment of my organization demands it.	☐	☐	☐	☐	☐
Con5 ...I seek conformity with the majority opinion on medical innovations.	☐	☐	☐	☐	☐

6. Power

I supported the adoption of the medical innovation in pharmacogenomics to...

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
P1 ...achieve professional recognition.	☐	☐	☐	☐	☐
P2 ...advance my career.	☐	☐	☐	☐	☐
P3 ...become established as a key opinion leader.	☐	☐	☐	☐	☐
P4 ...have an impact on decision makers.	☐	☐	☐	☐	☐
P5 ...increase my personal future earnings	☐	☐	☐	☐	☐
P6 ...benefit from first-hand information.	☐	☐	☐	☐	☐

7. Hedonic of pharmacogenomics

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
H1 ...I am always up to date on the last medical innovations.	☐	☐	☐	☐	☐
H2 ...Acquiring medical innovations gives me a good feeling.	☐	☐	☐	☐	☐
H3 ...Adopting medical innovations makes my work as a provider more exciting and stimulating.	☐	☐	☐	☐	☐
H4 ...I enjoy using the latest medical technologies.	☐	☐	☐	☐	☐
H5 ...I am enthusiastic about testing how medical innovations work for myself.	☐	☐	☐	☐	☐

8. Patient Benefit from pharmacogenomics

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
PB1 ...If I was convinced that a certain medical innovation would benefit patients, I would adopt it – even if it came at high cost.	☐	☐	☐	☐	☐
PB2 ...If a medical innovation increased patients' comfort, I would adopt it- even if this would mean increased effort on my part.	☐	☐	☐	☐	☐
PB3 ...I often seek information about medical innovations in my leisure time to find ways to increase patient well-being.	☐	☐	☐	☐	☐
PB4 ...If I was sure that a medical innovation would improve patient care, I would adopt it – even if there was a negative Health Technology Assessment (HTA) recommendation for this subgroup.	☐	☐	☐	☐	☐

9. Cognitive from pharmacogenomics

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
Cog1 ...I like to adopt medical innovations that satisfy my analytical mind.	☐	☐	☐	☐	☐
Cog2 ...I like to adopt medical innovations that challenge me intellectually.	☐	☐	☐	☐	☐
Cog3 ...I like to adopt medical innovations that improve my medical and intellectual skills.	☐	☐	☐	☐	☐
Cog4 ...I like to adopt medical innovations that demand logical thinking.	☐	☐	☐	☐	☐

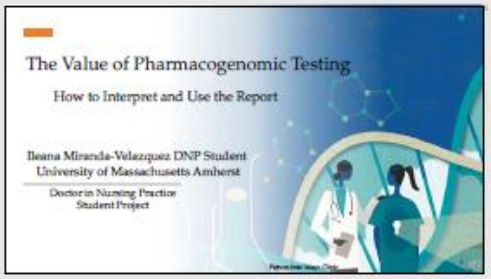
10. Please share any other comments you have below:

Hatz, M. H. M., Sonnenschein, T., Blankart, C. R. (2017). The PMA Scale: A measure of Physicians' motivation to adopt medical devices. Value in Health, 20, 533 – 541. http://doi.org/10.1016/j.jval.2016.12.002 (Adapted with permission). Logo picture from Synergy Rx.

Appendix G

Providers Pharmacogenomic Education

The Value of Pharmacogenomics



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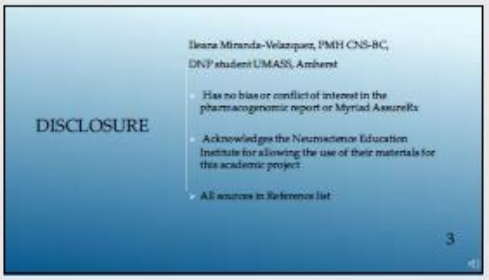

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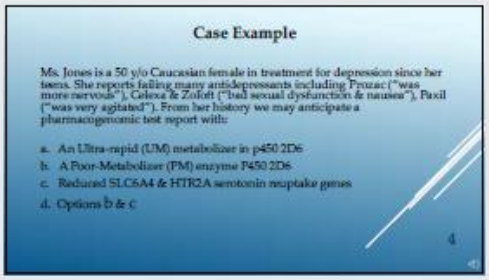

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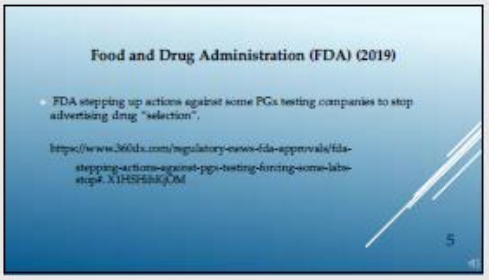

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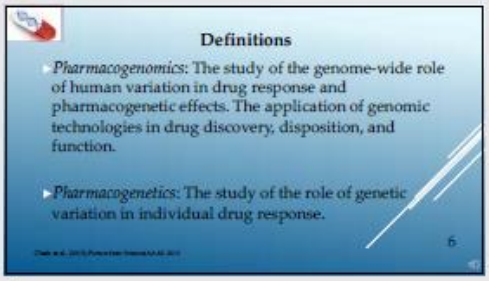


6

The Value of Pharmacogenomics

Definitions (continued)

- *Genotype*: The underlying genetic constitution of an individual.
- *Phenotype*: The observable outcome of the interaction of an individual's genes and environmental factors.
- *Polymorphism*: A gene is polymorphic if more than one allele occupies that gene's DNA sequence or length within a population. Generally, the specific difference must have a frequency of 1% in the population to be considered polymorphic.

7

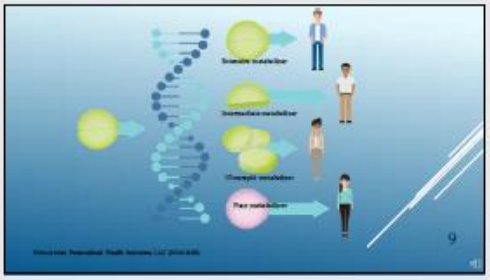
7

Genotypes that Affect Drug Metabolism

- PM: Poor metabolizers or inhibitors of P450 may have increased drug serum levels and adverse events
- IM: Intermediate metabolizers or inhibitors of P450 may have increased drug serum and adverse events
- EM (Normal): Extensive metabolizers metabolize substrates normally
- UM: Ultra-rapid metabolizers or inducers of P450 may have reduced drug serum levels and poor efficacy

8

8



9

9

The Value of PGx Testing

Past
- History of significant side effects on certain medications

Present
- Which antidepressant?
- Starting dose?
- Target dose?
- Maximum dose?

Future
- Which antidepressants and/or adjunctive treatments?

10

10

Six Areas to Test

Pharmacokinetics
- Cytochrome P450 Liver enzymes
- UGTs
- *Blood-brain barrier transporters (e.g., P-glycoprotein)

Pharmacodynamics
- Serotonin transporter (5-HTT or SERT)
- Post-synaptic receptors (5-HT2A, *5-HT2C)
- Human Leucocyte Antigen (HLA)

11

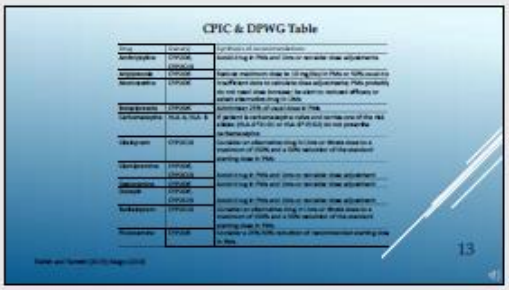
11

CPIC & DPWG Recommendations for Relevant Psychotropics and Cytochrome P450 enzymes

12

12

The Value of Pharmacogenomics



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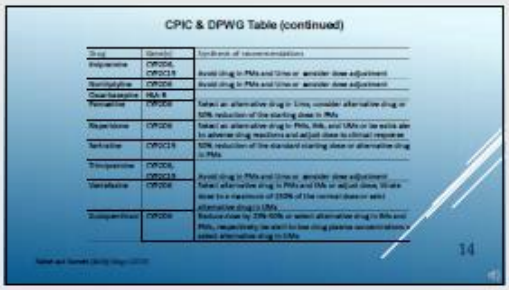

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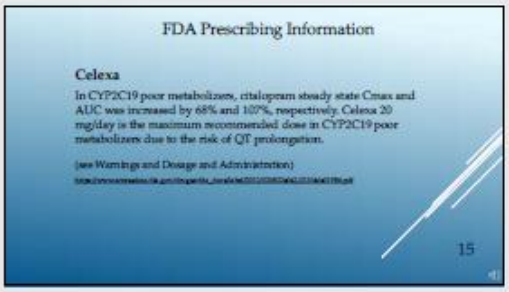

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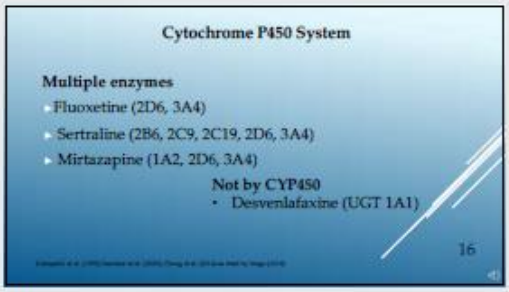

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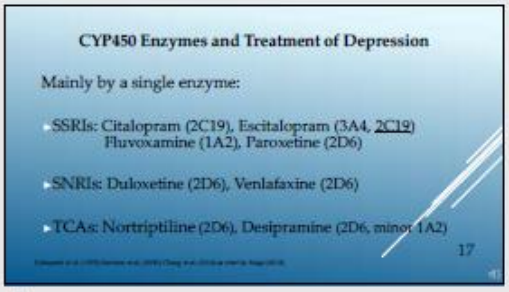

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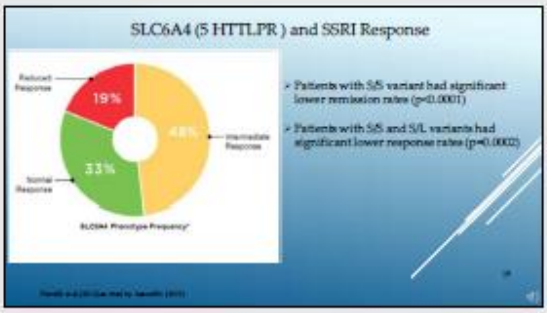
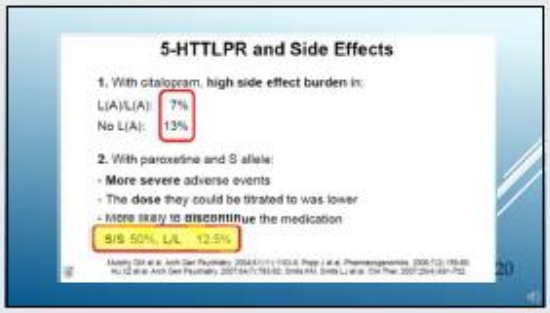
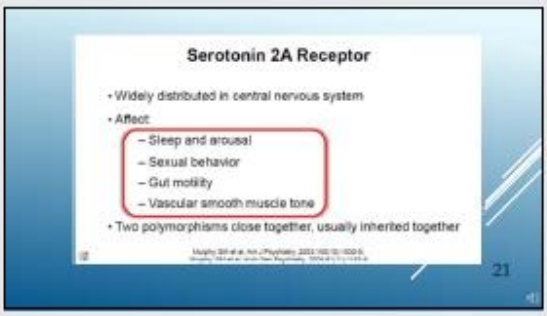
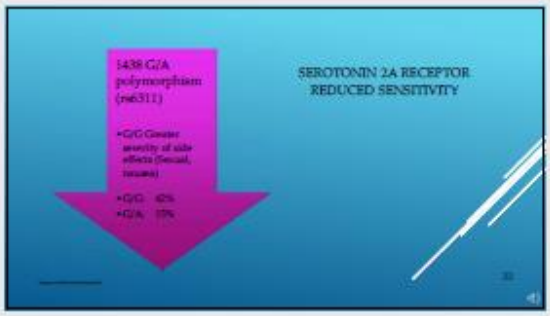
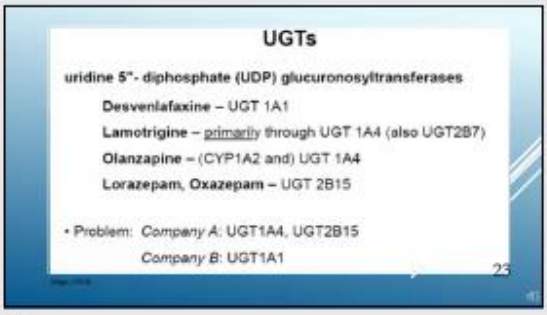
The Value of Pharmacogenomics

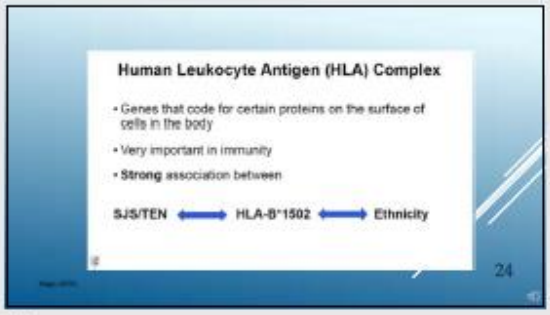




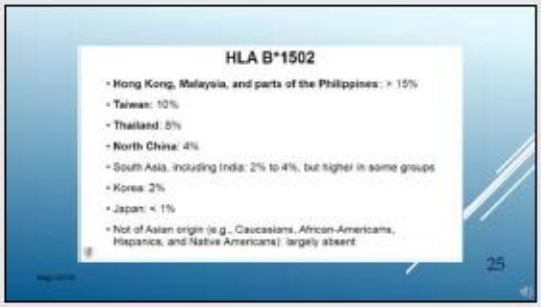








The Value of Pharmacogenomics



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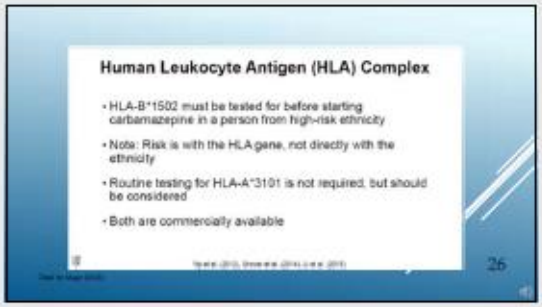

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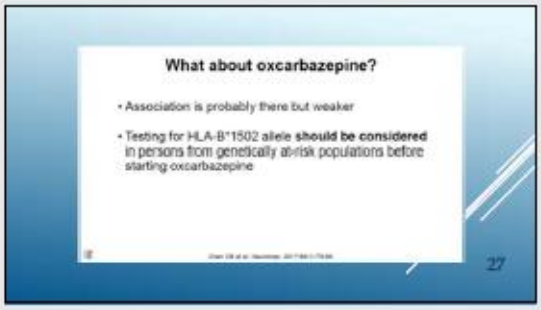

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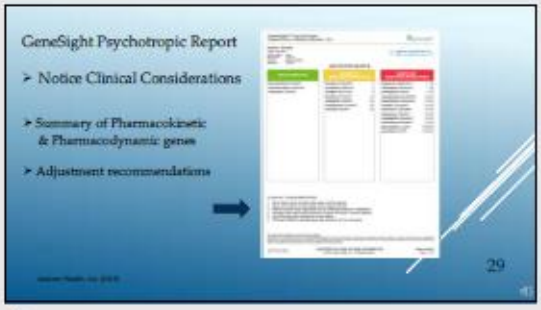

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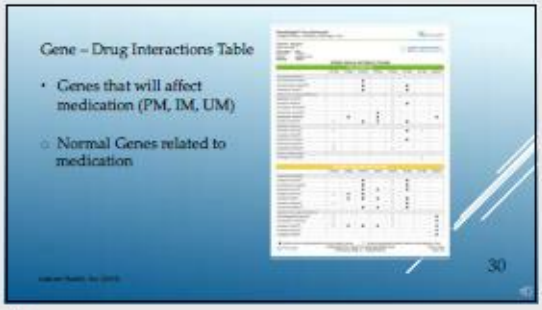

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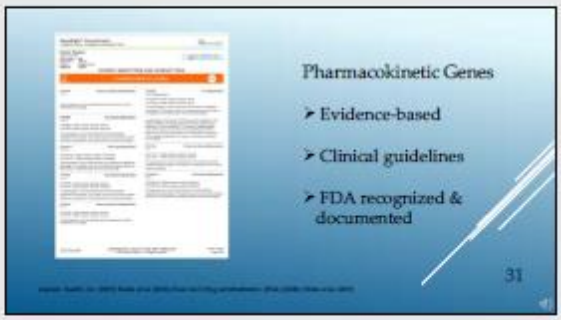
The Value of Pharmacogenomics



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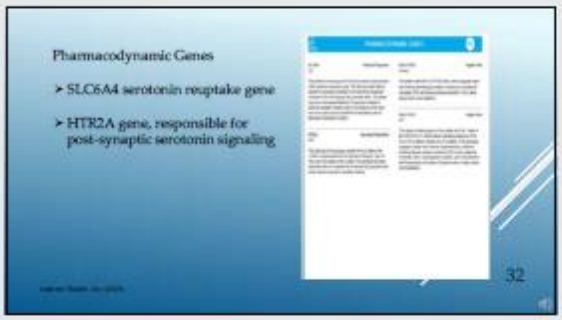

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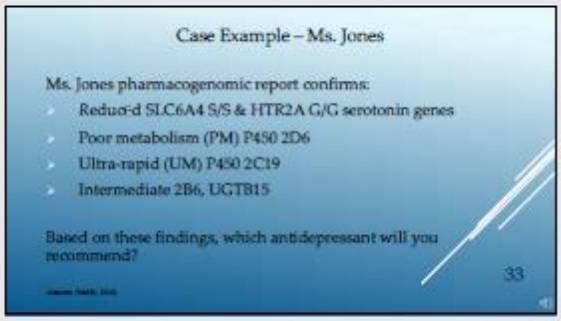

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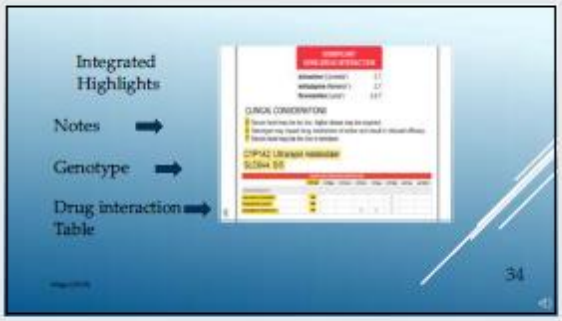

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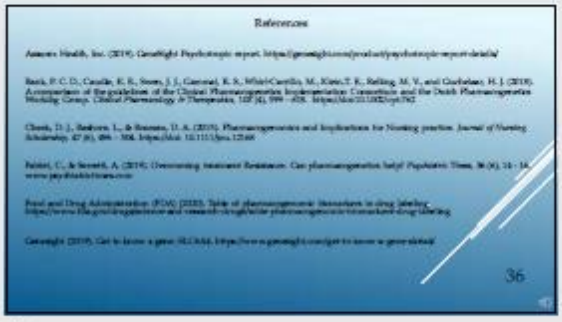

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Appendix H

Provider Motivation Adoption Post – Scale (PMA)

Provider Motivation Adoption Post - Scale (PMA)

Please rank the OPEN statements below based on your preference to adopt medical innovation.

1. What is your profession?

- Physician
- Nurse
- Clinical Therapist
- Administrator

2. What is your age?

- 25 to 34
- 35 to 44
- 45 to 54
- 55 to 64
- 65 to 74+

3. What is your gender?

- Female
- Male
- Other

4. Functional

I supported the adoption of medical innovation in pharmacogenomics because…

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
F1 ...is more reliable than existing technologies.	☐	☐	☐	☐	☐
F2 ...it saves time.	☐	☐	☐	☐	☐
F3 ...is more practical.	☐	☐	☐	☐	☐
F4 ...it facilitates procedures.	☐	☐	☐	☐	☐

5. Conformity

I supported the adoption of medical innovation in pharmacogenomics because...

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
Con1 ...my colleagues in my organization expect me to do so.	☐	☐	☐	☐	☐
Con2 ...my peers advise me to do so.	☐	☐	☐	☐	☐
Con3 ...all of my peers are using it.	☐	☐	☐	☐	☐
Con4 ...the competitive environment of my organization demands it.	☐	☐	☐	☐	☐
Con5 ...I seek conformity with the majority opinion on medical innovations.	☐	☐	☐	☐	☐

6. Power

I supported the adoption of the medical innovation in pharmacogenomics to...

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
P1 ...achieve professional recognition.	☐	☐	☐	☐	☐
P2 ...advance my career.	☐	☐	☐	☐	☐
P3 ...become established as a key opinion leader.	☐	☐	☐	☐	☐
P4 ...have an impact on decision makers.	☐	☐	☐	☐	☐
P5 ...increase my personal future earnings	☐	☐	☐	☐	☐
P6 ...benefit from first-hand information.	☐	☐	☐	☐	☐

7. Hedonic of pharmacogenomics

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
H1 ...I am always up to date on the last medical innovations.	☐	☐	☐	☐	☐
H2 ...Acquiring medical innovations gives me a good feeling.	☐	☐	☐	☐	☐
H3 ...Adopting medical innovations makes my work as a provider more exciting and stimulating.	☐	☐	☐	☐	☐
H4 ...I enjoy using the latest medical technologies.	☐	☐	☐	☐	☐
H5 ...I am enthusiastic about testing how medical innovations work for myself.	☐	☐	☐	☐	☐

8. Patient Benefit from pharmacogenomics

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
PB1 ...If I was convinced that a certain medical innovation would benefit patients, I would adopt it – even if it came at high cost.	☐	☐	☐	☐	☐
PB2 ...If a medical innovation increased patients' comfort, I would adopt it- even if this would mean increased effort on my part.	☐	☐	☐	☐	☐
PB3 ...I often seek information about medical innovations in my leisure time to find ways to increase patient well-being.	☐	☐	☐	☐	☐
PB4 ...If I was sure that a medical innovation would improve patient care, I would adopt it – even if there was a negative Health Technology Assessment (HTA) recommendation for this subgroup.	☐	☐	☐	☐	☐

9. Cognitive from pharmacogenomics

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
Cog1 ...I like to adopt medical innovations that satisfy my analytical mind.	☐	☐	☐	☐	☐
Cog2 ...I like to adopt medical innovations that challenge me intellectually.	☐	☐	☐	☐	☐
Cog3 ...I like to adopt medical innovations that improve my medical and intellectual skills.	☐	☐	☐	☐	☐
Cog4 ...I like to adopt medical innovations that demand logical thinking.	☐	☐	☐	☐	☐

10. Comments (no characters limit):

Hatz, M. H. M., Sonnenschein, T., Blankart, C. R. (2017). The PMA Scale: A measure of Physicians' motivation to adopt medical devices. Value in Health, 20, 533 – 541. http://doi.org/10.1016/j.jval.2016.12.002 (Adapted with permission)

Appendix I

Patient Health Questionnaire 9 (PHQ-9)

Patient Name: _____ Date: _____

Dear Patient,

In an effort to provide the highest standard of care and meet the requirements of your insurance company, we ask that you fill out the form below. This form is used as a screening tool for depression. Your provider will discuss the form with you during your visit. Thank you for your cooperation and the opportunity to care for you.

Over the ***last 2 weeks***, how often have you been bothered by any of the following problems?
(Please check)

	Not at all 0	Several days 1	More than half the days 2	Nearly every day 3
1. Little interest or pleasure in doing things	☐	☐	☐	☐
2. Feeling down, depressed, or hopeless.	☐	☐	☐	☐
3. Trouble falling/staying asleep, sleeping too much.	☐	☐	☐	☐
4. Feeling tired or having little energy.	☐	☐	☐	☐
5. Poor appetite or overeating.	☐	☐	☐	☐
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family. down.	☐	☐	☐	☐
7. Trouble concentrating on things, such as reading the newspaper or watching television.	☐	☐	☐	☐
8. Moving or speaking so slowly that other people could have noticed. Or the opposite, being so fidgety or restless that you have been moving around a lot more than usual.	☐	☐	☐	☐
9. Thoughts that you would be better off dead or of hurting yourself in some way.	☐	☐	☐	☐

---

10. If you checked off any problem on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
☐	☐	☐	☐

Appendix J

Email Communications With PMA Scale Author

Physician Motivation Adoption Scale - Communication with Author

---

From: Ileana
Sent: Monday, February 10, 2020 12:14 PM
To: Blankart Rudolf
Subject: RE: AW: Physician Motivation Adoption Scale (PMA)

Dear Dr. Blankart,
Thank you for thoughts and recommendations. Will share with you if I continue moving forward with the scale.

Muchas gracias,
Ileana

Sent from Mail for Windows 10

From: Blankart Rudolf
Sent: Sunday, February 9, 2020 7:16 AM
To: Ileana
Subject: AW: Physician Motivation Adoption Scale (PMA)

Dear Ilena

Thank you very much for reaching out.
Please find the paper of the PMA scale attached. You find the final scale in table 5 that you may directly integrate in your survey with a five-point Likert
scales with response options: strongly disagree, disagree, neutral, agree, and strongly agree.
The scale let you then identify whether adoption of your pharmacogenomic test is driven by the functional, conformity, power, hedonic, patient benefit or cognitive dimensions. That's an interesting question as adoption of testing is probably less driven by the cognitive and hedonic dimensions and probably more driven by the functional and maybe power dimensions compared to medical devices such as hip implants or heart valves.

I hope that helps.

Best wishes

Rudolf

Von: Ileana [mailto:imirandavela@umass.edu]
Gesendet: Samstag, 8. Februar 2020 18:16
An: Blankart Rudolf <Rudolf.Blankart@kpm.unibe.ch>
Betreff: Physician Motivation Adoption Scale (PMA)

Dear Dr. Blankart:

My name is Ileana Miranda-Velazquez, I am a Psychiatric Clinical Nurse Specialist of over 20 years of experience. I am doing the Doctor in Nursing Practice online program at the University of Massachusetts, Amherst, MA USA. I am planning to implement pharmacogenomics testing to the treatment of resistant Depression patients in a local Community Mental Health agency.

In my research I found the PMA scale which I am interested to apply to the agency physicians were I will implement my translational project. As you now, is difficult to get physicians on board with new technology. Pharmacogenomic testing is not a device, but is a laboratory technology that is increasing in strength world wide.

I will like your input about my thoughts. I have not found other scales that will measure physicians attitudes toward new technology. I believe the PMA will be a good match to my project. Will like to get a copy of the scale and how to use it.

Appreciate your time and wisdom,

Sincerely,

Ileana Miranda-Velazquez, PMH CNS-BC

Sent from Mail for Windows 10

Appendix K

Neuroscience Education Institute Authorization

From: Neuroscience Education Institute
Sent: Friday, June 19, 2020 12:06 PM
To: Ileana
Subject: Re: Dr. Stahl Teleconference

Dear Ileana,

Glad to hear it! Thank you.

Kind regards,
Edda
Neuroscience Education Institute
5900 La Place Court, Suite 120
Carlsbad, CA 92008
(888) 535-5600
customerservice@neiglobal.com
Hours: Mon - Fri, 8:00 am - 5:00 pm (Pacific time)

Tell us about your Customer Service Experience!

Neuroscience Education Institute

On Thu, Jun 18, 2020 at 4:26 PM Ileana <imirandavela@umass.edu> wrote:

> Hi Edda:
>
> These are great news to be able to use such a great source of information!!
>
> It will be my pleasure to share my results of my project with NEI at the end of my project.
>
> Deeply grateful,
>
> Ileana
>
> Sent from Mail for Windows 10

From: Neuroscience Education Institute
Sent: Thursday, June 18, 2020 7:08 PM
To: Ileana
Subject: Re: Dr. Stahl Teleconference

Hello Ileana,

Thank you for your email. Since it appears your inquiry regarding content will be to be limited to a few people and is purely educational in nature, we will allow you to use the content in slides, PDFs, references, etc. all of which you can access as a member from our website. We will also allow for you to play recorded webcasts from your NEI account and share it during a presentation. I hope this helps. Should you have any questions please let us know.

Kind regards,

Edda

Neuroscience Education Institute

5900 La Place Court, Suite 120

Carlsbad, CA 92008
(888) 535-5600

customerservice@neiglobal.com

Hours: Mon - Fri, 8:00 am - 5:00 pm (Pacific time)

Tell us about your Customer Service Experience!

Neuroscience Education Institute

Appendix L

Excel Data Model

Pre PHQ 9	Post PHQ 9	Age	Gender	Race	Ethnicity	Dx	Comorbid Pers	Subs Use Hx	#Med Pre PGx	#Med Post PGx	SLC 6A4	HTR 2A	CYP 1A2	CYP 2B6	CYP2 C19	CYP 2C9	CYP 2D6	CYP 3A4	UGT 1A4	UGT 2B15

Appendix M

Agency Approval letter

servicenet
innovative mental health and human services

April 1, 2020

ServiceNet, Inc.
50 Pleasant street
Northampton, MA 01060

To whom it may concern:

ServiceNet is pleased to support the proposed Doctor in Nursing Practice (DNP) quality improvement (QI) project: The Value of Pharmacogenomic Testing in Adults with Major Depression. Our agency agrees that the student Ms. Ileana Miranda Velazquez will review selected records within HIPPA guidelines to obtain data that will improve patients' treatment outcomes. We will also offer the administrative support for the assessment of our providers motivation to use innovative treatments and education in the area of pharmacogenomics.

The project is expected to start during the Fall 2020 after the approval from the University of Massachusetts, Amherst (UMass) Internal Review Board (IRB) and our Board of Directors.

Our agency is committed to provide mental health and human services through innovation "grounded in research and fueled by creativity". We are excited that this project will offer more insight about the benefits of pharmacogenomics in patient care and improve our caregivers' motivation in its use.

Respectfully,

Karen S. Franklin, LICSW
Vice President of Outpatient Services
ServiceNet
50 Pleasant St.
Northampton, MA 01060
413-584-6855 Office
413-585-1355 Fax